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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,424	05/22/2000	Darrell R. Anderson	012712-855	2393

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/10/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/576424	ANDERSON
	Examiner	Art Unit
	GAMBEL	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on 11/29/01

2a)☐ This action is FINAL. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-33

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 1-10, 13-18, 21-26

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 11-12, 19-20, 27-33

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☑ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☑ objected to by the Examiner. SEE OFFICE ACTION

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☑ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's election of the additional immunosuppressant CTLA-4 / CTLA4-Ig in Paper No. 22, filed 10/29/02, is acknowledged.

Given applicant's previous elections, the election reads on claims 11-12, 19-20 and 27-33 as they read on methods of treating the inflammatory condition Crohn's disease with anti-B7.1 antibodies alone in combination with CTLA-4 / CTLA4-Ig.

Claims 1-10, 13-18 and 21-26 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected inventions.

2. Applicant should amend the first line of the specification to update the status of the priority documents.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

4. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

5. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

Also the Brief Description of the Drawings should disclose the appropriate SEQ ID NOS for those drawings that include nucleic acid or amino acid sequences.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

6. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks (e.g. SEPHAROSE) should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

7. The filing date of the instant claims 12 and 20 with respect to the recitation of "humanized antibody" is deemed to be the filing date of the instant application USSN 09/576,424, filed 5/22/00), as the previous priority applications USSNs 08/746,361 and 08/487,550 do not appear to provide sufficient written support for the claimed limitation of "humanized antibody" in the instant application.

If applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the earlier priority applications. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

8. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: "humanized" antibody does not appear to have proper antecedent basis to the instant specification.

Alternatively, applicant is invited to provide direction for the written description of "humanized antibody" in the instant specification.

10. Claims 30-31 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "another entity that modulates the B7/CD28 pathway"

While the specification appears to provide written support for "moieties" and "immunosuppressants", applicant's amendments do provide sufficient written description nor set forth the metes and bounds of the term "another entity that modulates the B7/CD28 pathway".

The term "entity" is not the same as "moiety" nor the same as "immunosuppressant". For example, pages 435 and 762 of the Webster's II Dictionary defines:

entity: 1. the fact of existence. 2. The existence of something considered apart from its properties. 3. something that exists as particular and discrete unit.

moiety: 1. a half. 2. a part, portion or share.

The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "entity (entities)", as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

Additionally, applicant is invited to amend the claims to avoid the recitation of either "entity" or "moiety". Applicant is invited to consider amending the claims to recite "immunosuppressant", as an appropriate term to define the class of additional inhibitors of the B7:CD28 pathway.

11. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claim 30 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description encompassing "another entity that modulates the B7/CD28 pathway" because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of the "entity" , are not set forth in the specification as filed, commensurate in scope with the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.
Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of known species of certain inhibitors that suppress (versus the claimed recitation of "modulate") the B7:CD28 interactions or pathway, yet the instant specification does not provide sufficient written description as to the structural features of said "another entity that modulates the B7/CD28 pathway" and the correlation between the chemical structure and the function of the genus of "another entity that modulates the B7/CD28 pathway". Applicant appears to rely upon the disclosure of limited examples of known inhibitors of the B7/CD28 pathway claim any "entity" with any structure.

A person of skill in the art would not know which structure(s) is (are) essential, which structure(s) is (are) non-essential for inhibiting the B7/CD28 pathway, encompassed by the claimed invention. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required.

For example, Skolnick et al. (Trends in Biotech., 18: 34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). In the absence of sufficient guidance and direction to the structural and functional analysis, applicant's reliance upon the certain known inhibitors of the B7/CD28 pathway disclosed as filed does not appear to provide sufficient written description of distinct molecules of known and unknown entities that modulate the B7/CD28 pathway, encompassed by the claimed invention.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "another entity that modulates the B7/CD28 pathway"; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

12. Claim 30 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain known inhibitors of the B7/CD28 pathway as disclosed in the specification as filed and recited in claim 31, including the elected species CTLA-4 / CTLA-4Ig, does not reasonably provide enablement for any "entity that modulates the B7/CD28 pathway".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies "another entity that modulates the B7/CD28 pathway" other than the known inhibitors disclosed in the specification as-filed that would enable that any "entity" that would be effective or predictive of inhibiting B7/CD28 interactions or pathway or of inhibiting Crohn's disease.

For example, since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. inhibit the B7/CD28 pathway or inhibit Crohn's disease) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from known inhibitors of the B7/CD28 pathway and, in turn, utilizing predicted structural determinations to ascertain binding or functional aspects of any "entity" and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant application, it is noted that various structures as well as mutations, substitutions and the like provide a range of activities, no all which are necessarily predictive of "another entity that modulates the B7/CD28 pathway". It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological activities.

A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences or structural elements of "another entity that modulates the B7/CD28 pathway". There is insufficient guidance to direct a person of skill in the art to select particular sequences or structural elements as essential for in vivo characterization of their therapeutic potential to inhibit the B7/CD28 pathway, including to inhibit Crohn's disease. A person of skill in the art could not predict which particular amino acid sequences or structural elements of "another entity that modulates the B7/CD28 pathway" are essential and could be used in the claimed therapeutic methods.

The success of state of the art structure-based strategies for inhibitor design is highly unpredictable. For example, Kuntz (Science 257:1078-1082, 1992) on page 1080, column 3, discloses that as little as 2% of compounds predicted to inhibit specific enzymatic or receptor systems actually show inhibition in the micromolar range. Kuntz further discloses that "optimization" of these compounds has proven even more problematic. Therefore, in view of the unpredictability in the art, and in view of the insufficient guidance and working examples in the specification, the quantity of experimentation required by one skilled in the art to practice the invention undue.

Because of the lack of sufficient guidance and predictability in determining which structural requirements or modifications would lead to "another entity that modulates the B7/CD28 pathway" and that the relationship between the sequence or structure of that entity and its tertiary structure to its activity to inhibit the B7/CD28 pathway was not well understood and was not predictable. For example, see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.). It would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of "another entity that modulates the B7/CD28 pathway" or to treat Crohn's disease".

Without sufficient guidance, the changes which can be made in the structure of another entity that modulates the B7/CD28 pathway" is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Applicant is invited to the limit the claimed "another entity that modulates the B7/CD28 pathway" to those inhibitors disclosed in the specification as filed and to those activities which can be readily measured.

Applicant is reminded to provide sufficient written support for any amended "limitations" to avoid new matter issues. See MPEP 714.02 and 2163.06

13. Claims 11-12, 19-20 and 27-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for anti-B7.1 antibodies that inhibit the binding of B7.1 to CD28 as well as inhibiting IL-2 production as disclosed in the specification as filed and exemplified by the 16C10 and 7C10 antibodies, does not reasonably provide enablement for any antibody that inhibits the binding of B cells and T cells via the B7.1/CD28 pathway, as recited in claim 11 or an anti-B7.1 antibody that does not inhibit the B7.1/CTLA-4 binding interaction, as recited in claim 27.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In order to achieve inhibition of the B7:CD28/CTLA-4 pathway with an anti-B7.1 antibody, particularly an anti-B7.1 antibody that does not block B7.1:CTLA-4 binding, the anti-B7.1 antibody must be able to target B7.1 expressing cells and must inhibit critical interactions and effector functions. In order to achieve such inhibition, particularly for treating an inflammatory condition such as the elected invention Crohn's disease or intestinal inflammation, the anti-B7.1 antibodies need to inhibit the binding of B7.1 to CD28 as well as inhibiting IL-2 production as disclosed in the specification as filed and exemplified by the 16C10 and 7C10 antibodies. The skilled artisan would not predict that anti-B7.1 antibodies could achieve the requisite immunosuppression in the claimed methods in the absence of certain inhibitory properties, particularly if the anti-B7.1 antibodies cannot inhibit B7.1 binding to CTLA-4.

Without such guidance, targeting B7.1 with anti-B7.1 antibodies to immunosuppress or to treat inflammatory conditions (as well as autoimmune conditions) including those associated with intestinal inflammation or Crohn's disease would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

14. Claims 30-31 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30-31 are indefinite in its recitation of "modulates" because it is ambiguous as to the nature, direction (positive or negative) or degree of said modulating.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 11 and 19 are rejected under 35 U.S.C. § 102(e) as being anticipated by Linsley et al. (U.S. Patent No. 5,844,095) (see entire document). Linsley et al. teach methods of blocking T cell interactions with B7 positive cells including suppressing immune responses in immunoproliferative diseases such as Crohn's disease and ulcerative colitis (see Summary of the Invention, Compositions of the Invention and Methods for Using the Compositions of the Invention) with anti-B7 antibodies as well as CTLA-4 / CTLA-4Ig. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods of inhibiting inflammatory conditions such as Crohn's disease with anti-B7 antibodies as the elected invention as well as CTLA-4. The B7 specificity taught by Linsley et al. is the B7.1 specificity of the elected invention. Although claims 11 and 13 do not require combination therapy, Linsley et al. Do teach the use of anti-B7 or CTLA-4 alone or in combination with other immunosuppressive agents to block B7-mediated interactions and to treat pathological conditions (see Methods for Using the Compositions of the Invention).

18. Claims 11-12 and 19-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Linsley et al. (U.S. Patent No. 5,84,095) in view of the art known practice to employ primatized, humanized and or human antibodies in therapeutic modalities as the time the invention was made, as acknowledged by pages 28-37 of the instant specification or as evidenced by Aruffo et al. (U.S. Patent No. 6,051,228).

The teachings of Linsley et al. are set forth above and differ from the claimed methods by not disclosing the well known use of primatized, humanized or human antibodies in human therapy.

Pages 28-37 of the instant specification discloses the well known practice by the ordinary artisan at the time the invention was made to employ primatized or human antibodies in therapeutic modalities, given their increase half-life and decreased immunogenicity in comparison to murine antibodies in the treatment of human pathological conditions.

For the same reasons of increasing half-life and decreasing immunogenicity of therapeutic antibodies, Aruffo et al. teach the well known use of humanized antibodies to B cell antigens for immunosuppression in humans (see entire document, including Detailed Description of the Invention).

One of ordinary skill in the art at the time the invention was made would have been motivated to select recombinant B7-specific antibodies such as primatized, humanized or human antibodies in order to reduce the immunogenicity and to increase the half-life of antagonistic anti-B7 antibodies in the treatment of human pathology, including Crohn's disease. From the teachings of the references and the well known practice of employing therapeutic recombinant antibodies in humans by the ordinary artisan, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

20. It appears that methods of administering antibodies anti-B7.1 that do not inhibit the B7.1/CTLA-4 binding interaction are free of the prior art.

21. No claim allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
January 9, 2003